

CHANGES IN CYTOKERATIN EXPRESSION PATTERNS IN THE RESPIRATORY TRACT OF RATS EXPOSED TO ROOM-AGED CIGARETTE SIDESTREAM SMOKE FOR 12 MONTHS

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We have investigated cytokeratin (CK) expression changes in epithelial cells of the rat nasal cavity, trachea, and lung as an indicator of epithelial cell differentiation changes following chronic inhalation exposure to room-aged cigarette sidestream smoke (RASS) at a total particulate matter (TPM) concentration of 12 µg/L. The exposure conditions and results of the biochemical and histopathological examinations have been published [1] as have CK changes at nose level 1 (just posterior to incisor) [2]. Most of the histomorphological changes were adaptive; and there was little indication of progression of effects after 12 months compared to 3 or 6 months of RASS inhalation [1]. With regard to CK expression (for details of the immunohistological procedures, see [3]), changes were seen not only in epithelial compartments that had histomorphological changes, but also in compartments that had no obvious histomorphological changes. Changes that had histomorphological correlates included increases in CK14 and CK15 in hyperplasia and squamous metaplasia of the nonciliated respiratory epithelium at nose level 1, intense staining for CK14 in focal atrophy and reserve cell hyperplasia of the olfactory epithelium at nose level 2 (at incisive papilla), and intense staining for CK7 in focal hyperplasia of the lung alveolar epithelium (also in untreated rats). Many of the CK expression changes that had no histomorphological correlates were decreases in specific CKs, e.g., of CK15 and CK18 in basal cells of the respiratory epithelium at nose level 2, or of CK19 in ciliated cells of the terminal bronchioli in the lung. Some of the CK changes seen after 12 months were comparable to those seen after 8 days of RASS exposure [4]. In conclusion, while the sensitivity of the CK expression analysis is high, the biological relevance of the changes that had no histomorphological correlates requires further investigation.

References: [1] Haussmann, H.-J. et al., *Inhal. Toxicol.* 10, 663-697 (1998); [2] Schlage, W.K. et al., *Toxicol. Letters* 96,97, 309-318 (1998) [3] Schlage, W.K., et al., *Toxicol. Pathol.* 26, 324-343 (1998); [4] Schlage, W.K. et al., *Toxicol. Pathol.* 26, 344-360 (1998)

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